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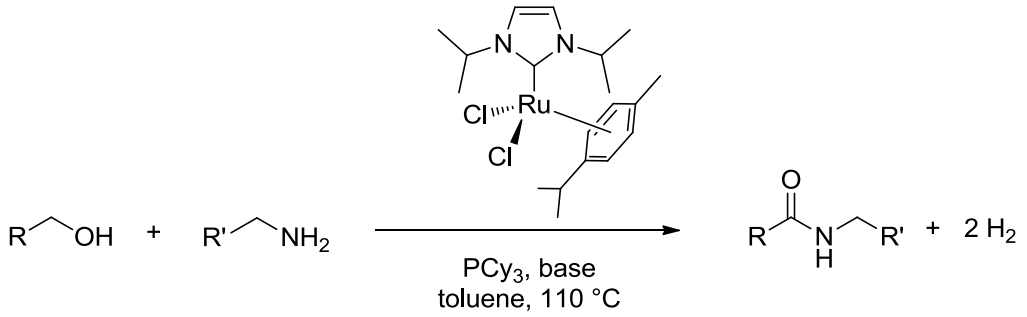
Mechanistic study of the ruthenium-catalyzed synthesis of amides from alcohols and amines

Ilya Makarov*, Peter Fristrup, Robert Madsen

Department of Chemistry, Technical University of Denmark, 2800 Lyngby, DENMARK

E-mail: ilym@kemi.dtu.dk
Webpage: http://www.organic.kemi.dtu.dk/

The amide bond is one of the most important linkages in organic chemistry and constitutes the key functional group in peptides, polymers and many pharmaceuticals [1]. Amides are often synthesized by coupling of carboxylic acids or its derivatives with amines. In spite of their efficiency these methods are not environmentally friendly since toxic reagents are used and a lot of waste is produced. Development of new synthetic methods which are both efficient and "green" continues to receive significant attraction. Recently in Madsen group a new method for amide synthesis has been discovered where alcohols and amines are coupled directly with the liberation of hydrogen [2, 3] (Scheme 1).



Scheme 1. Amide synthesis.

In the present work the mechanistic studies of this reaction have been carried out. The studies are divided into an experimental part and a theoretical part. In the experimental part reaction kinetics was studied. Para-substituted benzyl alcohols were used as substrates to elucidate the electronic influence of the para substituent on the reactivity, *i.e.* a Hammett study. By using DFT calculations with the B3LYP or M06 functionals Gibbs free energies and structures were determined for some metal complexes and transition states in the proposed catalytic cycle. From the experimental and theoretical studies the rate determining step will be established which is important to further optimize the reaction.

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